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Antibody-free LC-MS/MS protein analysis of TRAIL

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Propositions accompanying the PhD thesis:

Antibody-free LC-MS/MS protein analysis of TRAIL

1. Antibody-free LC-MS/MS will play a more important role in protein bioanalysis due to the increasing number of protein drugs currently in development. This will reduce the time needed for method development, which will reduce the amount of time needed for raising specific antibodies for ligand binding assays. This is currently a lengthy procedure that often has an uncertain outcome. *(This thesis)*

2. LC-MS/MS protein analysis combined with SPE protein enrichment provides extensive multiplexing capabilities compared to ligand binding assays. This is beneficial for the screening of multiple closely related recombinant protein variants or combination therapies in clinical research. *(This thesis)*

3. A systematic evaluation of antibody-free workflows is required in order to gain a better understanding of the relation between the physico-chemical properties of an analyte and its analytical behavior. *(This thesis)*

4. Although a lot of knowledge about preparative-scale protein purification has been acquired over the years, this knowledge has still not been fully exploited for analytical-scale applications. *(This thesis)*

5. Much knowledge about peptide enrichment can be derived from the vast amount of bioanalytical literature for small molecules. However, it is of importance to realize that the matrix is much more complex after digestion in comparison to the corresponding undigested sample. *(This thesis)*

6. The industry focuses on expressing and purifying biopharmaceutical proteins, but it should also focus on providing stable-isotope-labelled proteins as internal standards. This will largely improve the quality of the performed bioanalysis during the (pre-) clinical phase in drug research. *(This thesis)*

7. A carefully optimized LC-MS/MS protein analysis method with the use of a proper internal standard can be validated according to the same current international guidelines used for the bioanalysis of small molecules. *(This thesis)*

8. Due to the increasing drug prices, especially of biopharmaceuticals: “hand clapping of science is now inextricably linked to hand wringing over affordability” (New Eng J Med 2015; 373(19): 1797-1799). Consequently, the demand for new biomarkers will strongly increase.

9. The most exciting phrase to hear in science, the one that heralds new discoveries, is not ‘Eureka!’ but ‘That’s funny’.
   Isaac Asimov

10. Nothing is a waste of time if you use the experience wisely.
    Auguste Rodin